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10/29/97

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
In re application of:

Cook and Manoharan

Serial No.: 08/117,363

Group Art Unit: 1807

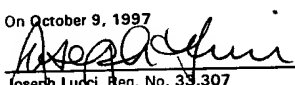
Filed: September 3, 1993

Examiner: S. Houtteman

For: AMINE-DERIVATIZED NUCLEOSIDES AND OLIGONUCLEOSIDES

I, Joseph Lucci, Registration No. 33,307 certify that this correspondence is being deposited with the U.S. Postal Service as First Class mail in an envelope addressed to the Commissioner of Patents and Trademarks, Washington, D.C. 20231.

On October 9, 1997


Joseph Lucci Reg. No. 33,307

Assistant Commissioner
For Patents
Washington, D.C. 20231

REQUEST FOR RECONSIDERATION

This responds to the Office Action mailed June 10, 1997, in connection with the above-identified patent application.

Claims 1-29 are pending in this patent application.

Claims 1-19 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting in view of claims 1-29 of co-pending application Serial No. 08/464,953. Applicants request that resolution of this rejection be deferred pending identification of allowable subject matter in the present patent application.

Claims 1, 2, 7, 13, 16, 17, 21, and 27 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Manoharan, et al., *Tetrahedron Letters* 1991, 32, 7171 ("the Manoharan reference"). Applicants respectfully request

reconsideration of this rejection, as the Manoharan reference is not prior art with respect to the claimed inventions. The Office Action asserts that the Manoharan reference is relevant to the claimed inventions due to its disclosure of a 2'-O-aminopentyl compound which can be functionalized with such moieties as biotin, fluorescein, cholic acid, and digoxigenin. Such compounds, however, are clearly disclosed in a patent application from which the present patent application claims priority, Application Serial No. 07/782,374 ("the 374 Application") (see, e.g., Example 8 thereof). In view of this claim of priority and the fact that 374 Application was filed with the U.S. Patent and Trademark Office on October 24, 1991, the Manoharan reference is not "a printed publication . . . more than one year prior to the date of application for patent in the United States," as required by Section 102(b). Indeed, the Manoharan reference was not published until 1991 and, thus, cannot possibly constitute Section 102(b) prior art with respect to the disclosure of the 374 Application.¹ In view of this fact, Applicants request that the rejection for alleged anticipation be reconsidered and withdrawn.

Claims 1-29 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over U.S. Patent No. 4,910,300 ("the Urdea patent") in view of U.S. Patent No. 4,743,535 ("the Carrico patent"), U.S. Patent No. 4,743,535 ("the Matteucci patent"),

¹ In fact, it is Applicants' understanding that the Manoharan reference did not publish until December of 1991, nearly two months after the filing date of the 374 Application.

International Patent Application WO 92/05186 ("the Matteucci reference"), and International Patent Application WO 91/14696 ("the Latham reference"). Applicants respectfully request reconsideration of this rejection, as it is predicated upon an incorrect reading of the Urdea patent. The basis for the rejection is an alleged disclosure of a 5'-O-amino nucleoside in Scheme I at columns 10-11 of the Urdea patent. The Office Action erroneously concludes that the Urdea patent provides such disclosure because some of the nucleosides shown in Scheme I bear an "R₁" substituent at their 5'-O- position, and because the patent allegedly defines "R₁" at column 4 as being an amine.² Applicants note, however, that the definition of R₁ at column 4 in no way relates to the structures shown in Scheme I, much less to the identity of substituents which are to be appended to the 5'-O-position of a nucleoside. Indeed, the definition of R₁ appearing at column 4 of the Urdea patent is explicitly said to relate to "the modified nucleotide of Formula 1." Formula 1, in turn, shows a R₁ substituent attached to a nucleosidic base and a *different* substituent, R₄, attached to the 5'-O-position. The Urdea patent teaches that R₄ should not be an amine but, rather, that "R₄ is typically hydrogen, if the modified nucleotide is a terminal 5' structure, or a suitable blocking group useful in polynucleotide synthesis." (Urdea patent at column 5, lines 21-

² The Office Action refers to the definition of R₁ at line 4 of column 4. It is believed that the Examiner intended to refer to lines 51-52 of column 4, since lines 51-52 refer to the R₁ group but line 4 does not.

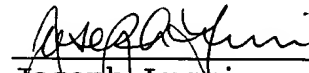
23). Thus, the appearance of R_1 in Scheme I is inconsistent with the overall teaching of the Urdea patent, and appears to nothing more than a typographical error. This is borne out by the fact that there appears to be a nominal change in the definition of the 5'-O-substituent (from R_1 to R') as one proceeds from the third intermediate in the Scheme (*i.e.*, the one at the bottom of column 10) to the fourth (*i.e.*, the one at the top of column 11), in spite of the fact that the reaction conditions said to be employed are not ones which would be expected to affect the 5'-O-position. There is, therefore, no basis for concluding that Scheme I, or any other portion of the Urdea patent, discloses placing an amine group at the 5'-O-position of a nucleoside. Since the rejection for alleged obviousness is predicated upon such a disclosure, Applicants respectfully request that the rejection be reconsidered and withdrawn.

ISIS-1169

PATENT

It is believed all of the claims presently before the Examiner patentably define the invention over the prior art and are otherwise in condition for ready allowance. An early Office Action to that effect is, therefore, earnestly solicited.

Respectfully submitted,



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Date: October 9, 1997

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